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Mouse PAR34 mature VH amino acid sequence (SEQ ID NO:2)

E I Q L Q Q S G P E L V K P G A S V K V
S C K A S G Y A F T N Y N M Y W V K Q S
H G K S L E W I G Y I D P Y Y G D P G Y
S Q K F K G K A T L T V D K S S S T A Y
M H L N S L T S E D S A V Y Y C A R R G
N F P Y Y F D Y W G Q G T T L T V S S

Mouse PAR34 mature VL amino acid sequence (SEQ ID NO:3)

D I K M T Q S P S S M Y A S L G E R V T
I T C K A S Q D I N S Y L S W F Q Q K P
G K S P K T L I Y R A N R L V D G V P S
R F S G S G S G Q D Y S L T I S S L E Y
E D M G I Y Y C L Q Y D E F P Y T F G G
G T K L E I K

Mouse PAR80 mature VH Region Amino Acid Sequence (SEQ ID NO:4)

E V Q L Q Q S G A E L V R S G A S V K L
S C T A S G F N I K D Y Y I H W V K Q R
P E Q G L E W I G C I D P E N G D T E Y
A P N F Q G R A T M T A D T S S N T A Y
L Q L S S L T S E D T A V Y Y C Y G G T
I T F A Y W G Q G T L V T V S A

Mouse PAR80 mature VL Region Amino Acid Sequence (SEQ ID NO: 5)

Q A V V T Q E S A L T T S P G E T V T L
T C R S S T G A V T T S N S A N W V Q E
K P D H L F T G L I G G T I N R V P G V
P A R F S G S L I G D K A A L T I T G A
Q T E D E A I Y F C A L W Y S N H W V F
G G G T K L T V L G

The CDRs based on the definition of Kabat are bolded and underlined.

FIG. 1

Panel of Monoclonal Antibodies Generated Against Human AR

ANTI-BODY	ISO-TYPE	BINDING						INHIBITION OF AR-EGFR INTER-ACTION	INHIBITION OF AR-MEDIATED PROLIFERATION (µg/ml)			
		AR	Surface AR	EGF	HB EGF	Cyno AR	Murine AR		3T3		HEKn	
									IC50%	IC90%	IC50%	IC90%
PAR2	IgG1, λ	+++	+++	-	-	+++	+++	++	0.13	1.3	0.35	>3
PAR 5	IgG1, λ	+++	+++	-	-	ND	+++	++	0.8	7.2	ND	ND
PAR15	IgG1, λ	+++	++	-	-	+++	+++	++	0.11	0.71	.2	>3
PAR19	IgG2b, κ	+++	+++	-	-	ND	-	++	5.9	>10	ND	ND
PAR22	IgG1, λ	+++	++	-	-	ND	+++	++	6.8	>10	ND	ND
PAR23	IgG1, λ	+++	++	-	-	ND	++	++	1.7	6.9	ND	ND
PAR26	IgG2b, κ	+++	+++	-	-	ND	-	++	>10	>10	>3	>3
PAR29	IgG1, λ	+++	+++	-	-	ND	+++	++	0.9	>10	ND	ND
PAR31	IgG2b, λ	+++	+++	-	-	+++	+++	++	0.7	1.9	.07	>3
PAR34	IgG2b, κ	+++	+++	-	-	+++	+++	++	0.072	0.71	.041	2.95
PAR44	IgG1, κ	+++	++	-	-	ND	+++	ND	4.1	>10	1.7	>3
PAR46	IgG1, κ	+++	++	-	-	ND	+++	ND	0.6	>10	ND	ND
PAR51	IgG1, λ	+++	++	-	-	ND	++	ND	4	>10	ND	ND
PAR67	IgG2b, κ	+++	++	-	-	+++	-	ND	>10	>10	>3	>3
PAR79	IgG1, κ	+++	++	-	-	ND	-	ND	2.8	>10	ND	ND
PAR80	IgG2a, λ	+++	+++	-	-	+++	-	ND	0.072	0.42	0.2	2.8
PAR81	IgG1, κ	+++	++	-	-	ND	-	ND	3.9	>10	ND	ND
PAR84	IgG2a, λ	+++	+++	-	-	+++	-	ND	0.51	0.8	0.48	>3

BINDING – direct binding as detected by ELISA

INHIBITION OF AR-EGFR INTERACTION – ability to inhibit AR binding to A431 (human EGFR+ epidermoid carcinoma)

INHIBITION OF PROLIFERATION – inhibition of proliferation of 3T3 (murine) cells to 100 ng exogenous human AR, or HEKn (human) cells to endogenously produced AR

ND – not determined; IC50% is the amount of the antibody needed to accomplish 50% inhibition; IC90% is the amount of the antibody needed to accomplish 90% inhibition

FIG. 2

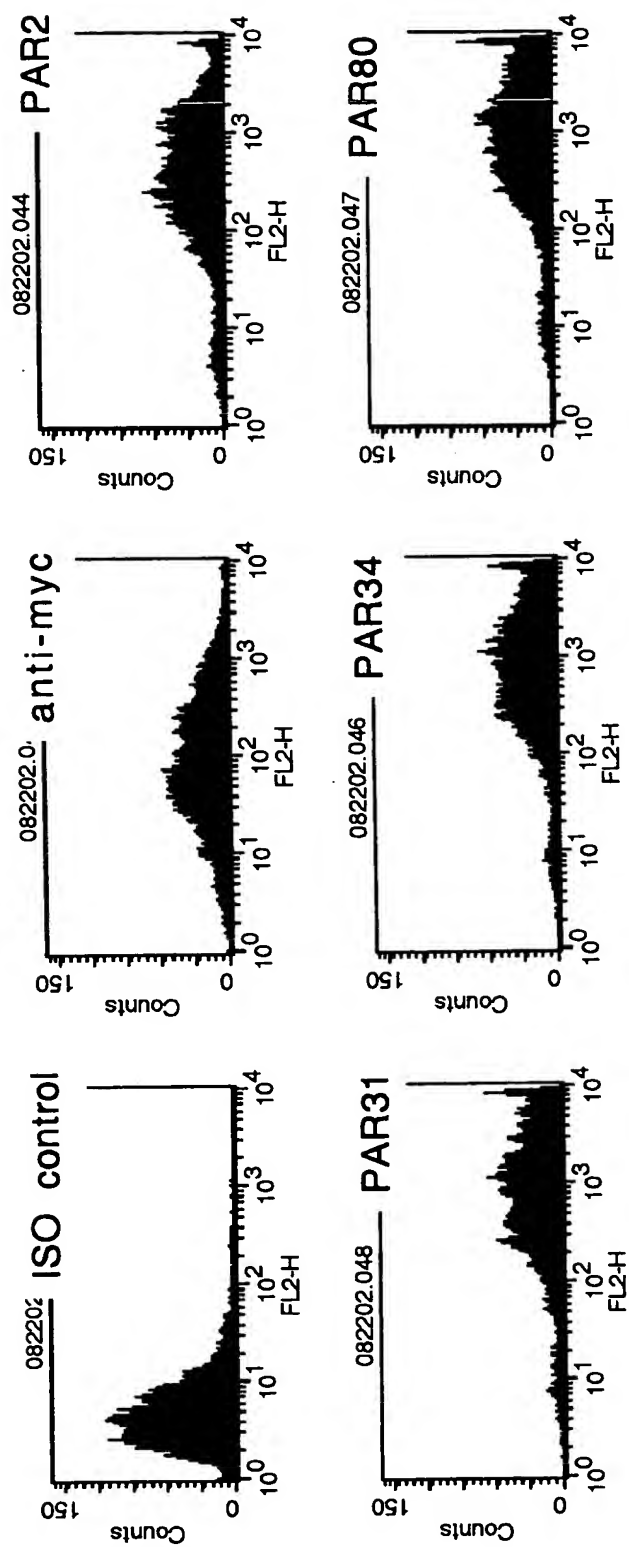


FIG. 3

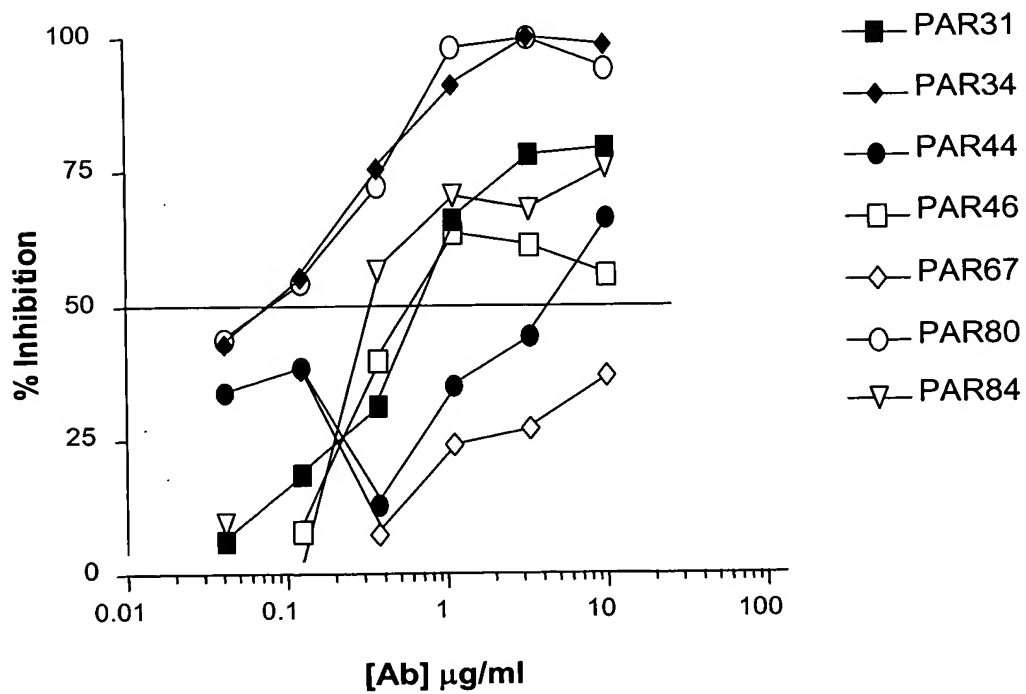
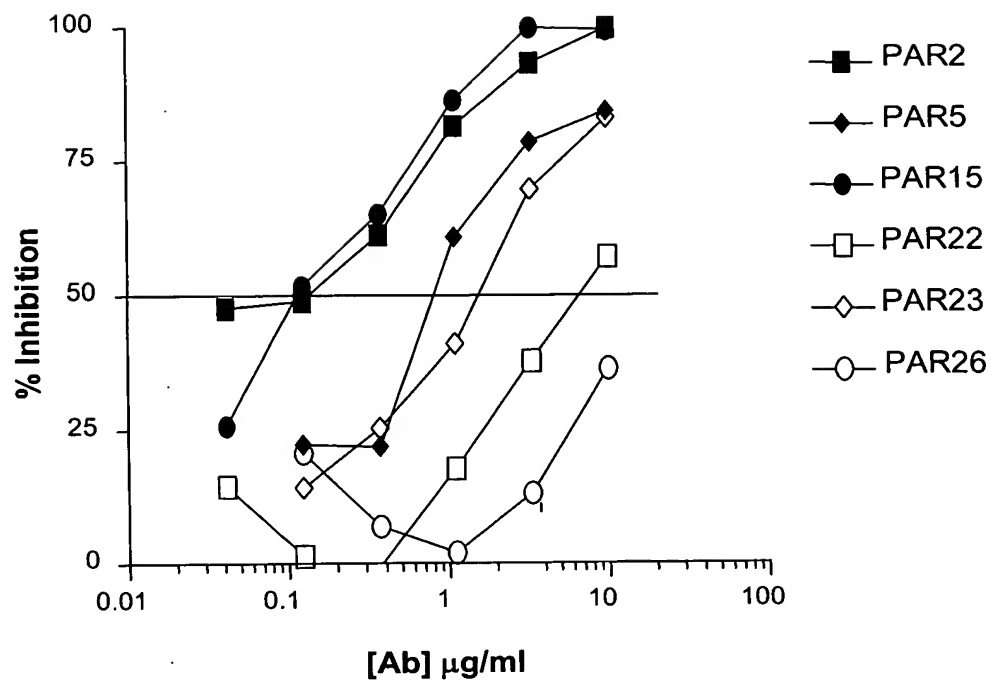


FIG. 4

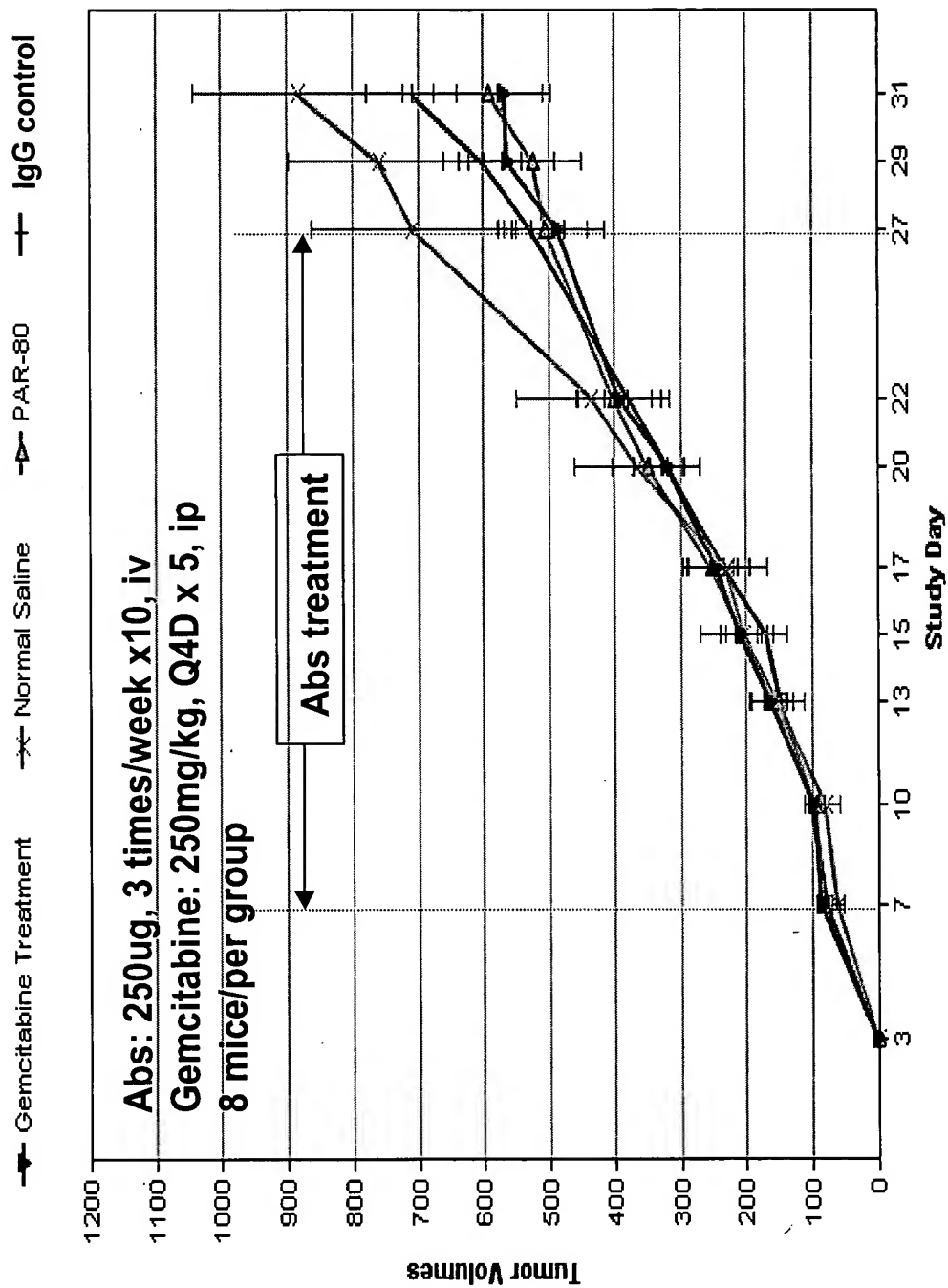


FIG. 5

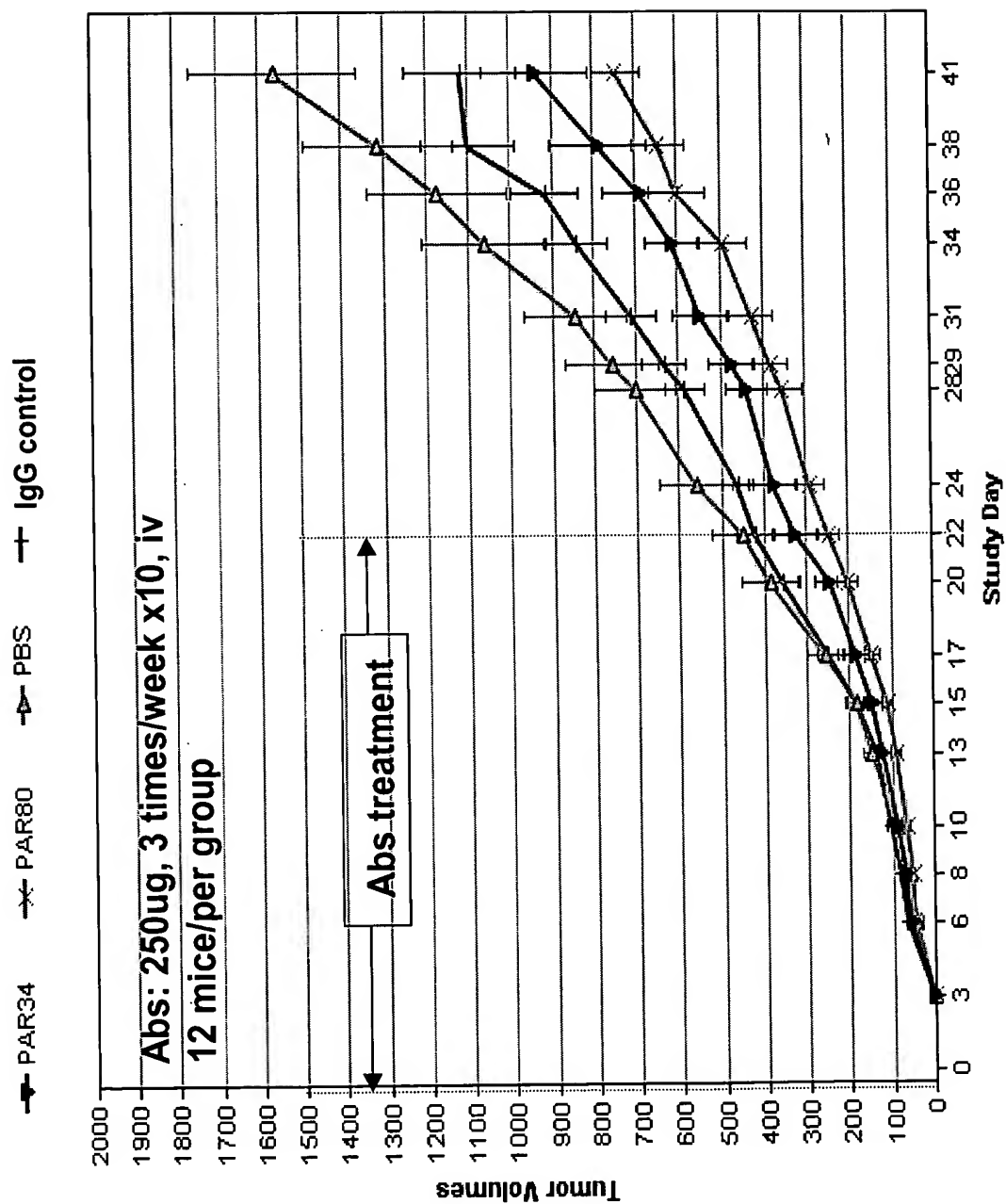


FIG. 6

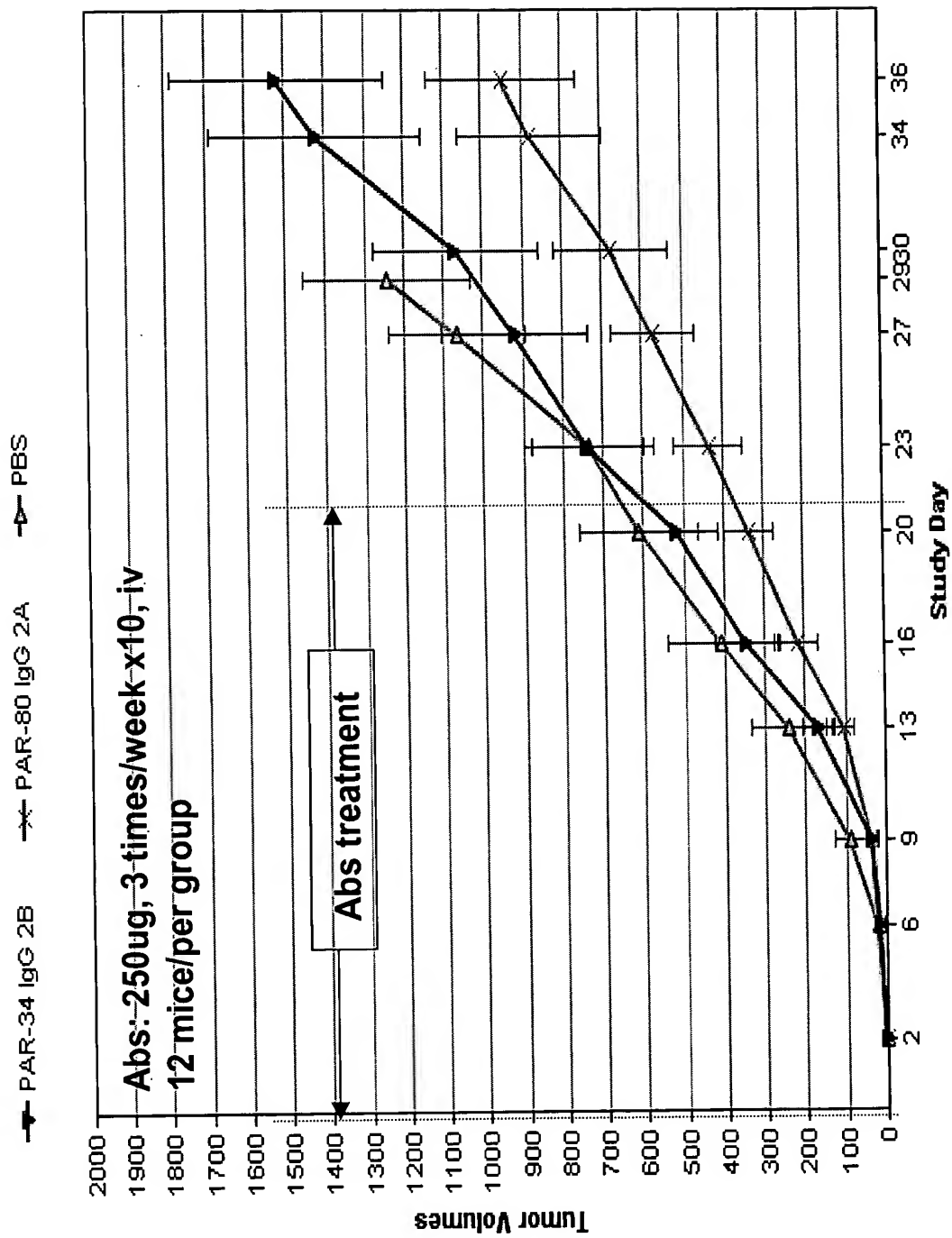


FIG. 7

cDNA (SEQ ID NO:8) and amino acid (SEQ ID NO:9) sequences for the signal peptide and heavy chain variable region of the PAR34 antibody.

```

                                     30                               60
ATGGAATGGAGATGGATCTTTCTCTTCCTGTCAGGAACTACAGGTGTCCACTCTGAG
M E W R W I F L F L L S G T T G V H S E

                                     90                               120
ATCCAGCTGCAGCAGTCTGGACCTGAGCTGGTGAAGCCTGGGGCTTCAGTGAAGGTATCC
I Q L Q Q S G P E L V K P G A S V K V S

                                     150                               180
TGCAAGGCTTCTGGTTATGCATTCACTAACTACAACATGTACTGGGTGAAGCAGAGCCAT
C K A S G Y A F T N Y N M Y W V K Q S H

                                     210                               240
GGAAAGAGCCTTGAGTGGATTGGATATATTGATCCTTACTATGGTGATCCTGGCTACAGC
G K S L E W I G Y I D P Y Y G D P G Y S

                                     270                               300
CAGAAGTTCAAGGGCAAGGCCACATTGACTGTTGACAAGTCCTCCAGCACAGCCTACATG
Q K F K G K A T L T V D K S S S T A Y M

                                     330                               360
CATCTCAACAGCCTGACATCTGAGGACTCTGCAGTCTATTACTGTGCAAGACGGGGTAAC
H L N S L T S E D S A V Y Y C A R R G N

                                     390                               414
TTCCCGTACTACTTTGACTACTGGGGCCAAGGCACCACTCTCACAGTCTCCTCA
F P Y Y F D Y W G Q G T T L T V S S
```

FIG. 8

cDNA (SEQ ID NO:10) and amino acid (SEQ ID NO:11) sequences for the signal peptide and light chain variable region of the PAR34 antibody.

```

                                     30                                     60
ATGAGGACCCCTGCTCAGTTTCTTGGAATCTTGTTGCTCTGGTTTCCAGGTATCAAATGT
M R T P A Q F L G I L L L W F P G I K C

                                     90                                     120
GACATCAAGATGACCCAGTCTCCATCTTCCATGTATGCATCTCTAGGAGAGAGAGTCACT
D I K M T Q S P S S M Y A S L G E R V T

                                     150                                     180
ATCACTTGCAAGGCGAGTCAGGACATTAATAGCTATTTAAGCTGGTTCCAGCAGAAACCA
I T C K A S Q D I N S Y L S W F Q Q K P

                                     210                                     240
GGGAAATCTCCTAAGACCCTGATCTATCGTGCAAACAGATTGGTAGATGGGGTCCCATCA
G K S P K T L I Y R A N R L V D G V P S

                                     270                                     300
AGGTTTCAGTGGCAGTGGATCTGGGCAAGATTATTCTCTCACCATCAGCAGCCTGGAGTAT
R F S G S G S G Q D Y S L T I S S L E Y

                                     330                                     360
GAAGATATGGGAATTTATTATTGTCTACAGTATGATGAGTTTCCGTACACGTTTCGGAGGG
E D M G I Y Y C L Q Y D E F P Y T F G G

                                     381
GGGACCAAGCTGGAAATAAAA
G T K L E I K
```

FIG. 9

Alignment of the VH region amino acid sequences of PAR34 (SEQ ID NO:2), HuPAR34 (SEQ ID NO:12), and the human germline DP-3/JH4 segments (SEQ ID NO:13).

		30
PAR34	E I Q L Q Q S G P E L V K P G A S V K V S C K A S G Y A F T	
HuPAR34	E V Q L V Q S G A E V K K P G A <u>S</u> V K I S C K V S G Y <u>A</u> F T	
DP-3	E V Q L V Q S G A E V K K P G A T V K I S C K V S G Y T F T	
		60
PAR34	<u>N Y N M Y</u> W V K Q S H G K S L E W I G <u>Y I D P Y Y G D P G Y</u>	
HuPAR34	<u>N Y N M Y</u> W V <u>R</u> Q A P G K G L E W <u>I</u> G <u>Y I D P Y Y G D P G Y</u>	
DP-3	- - - - - W V Q Q A P G K G L E W M G - - - - -	
		90
PAR34	<u>S Q K F K G</u> K A T L T V D K S S S T A Y M H L N S L T S E D	
HuPAR34	<u>S Q K F K G</u> <u>K A</u> T <u>L</u> T <u>V</u> D <u>K</u> S T <u>S</u> T A Y M E L S S L R S E D	
DP-3	- - - - - R V T I T A D T S T D T A Y M E L S S L R S E D	
		119
PAR34	S A V Y Y C A R <u>R G N F P Y Y F D Y</u> W G Q G T T L T V S S	
HuPAR34	T A V Y Y C A R <u>R G N F P Y Y F D Y</u> W G Q G T L V T V S S	
DP-3/JH4	T A V Y Y C A T - - - - - W G Q G T L V T V S S	

FIG. 10

		30
PAR34	D I K M T Q S P S S M Y A S L G E R V T I T C <u>K A S Q D I N</u>	
HuPAR34	D I Q M T Q S P S S L S A S V G D R V T I T C <u>K A S Q D I N</u>	
L1	D I Q M T Q S P S S L S A S V G D R V T I T C - - - - - - -	
		60
PAR34	<u>S Y L S</u> W F Q Q K P G K S P K T L I Y <u>R A N R L V D</u> G V P S	
HuPAR34	<u>S Y L S</u> W F Q Q K P G K A P K <u>T L I Y</u> <u>R A N R L V D</u> G V P S	
L1	- - - - W F Q Q K P G K A P K <u>S L I Y</u> - - - - - - - G V P S	
		90
PAR34	R F S G S G S G Q D Y S L T I S S L E Y E D M G I Y Y C <u>L Q</u>	
HuPAR34	R F S G S G S G <u>Q D Y</u> T L T I S S L Q P E D F A T Y Y C <u>L Q</u>	
L1	R F S G S G S G T D F T L T I S S L Q P E D F A T Y Y C - -	
		107
PAR34	<u>Y D E F P Y T</u> F G G G T K L E I K	
HuPAR34	<u>Y D E F P Y T</u> F G G G T K V E I K	
Jk4	- - - - - - - F G G G T K V E I K	

Nucleotide sequence (SEQ ID NO:16) and deduced amino acid sequence (SEQ ID NO:17) of the heavy chain variable region (including the signal peptide sequence) of HuPAR34 in the mini exon.

```

                                     30                               60
ACGCGTCCACCATGGAATGGAGATGGATCTTTCTCTTCCTCCTGTCAGGAACTACAGGTG
      M E W R W I F L F L L S G T T G

                                     90                               120
TCCACTCTGAGGTCCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAGCCTGGGGCTTCTG
V H S E V Q L V Q S G A E V K K P G A S

                                     150                               180
TGAAAATATCCTGCAAGGTTTCTGGTTATGCATTCACTAACTACAACATGTATTGGGTGA
V K I S C K V S G Y A F T N Y N M Y W V

                                     210                               240
GGCAGGCCCTTGAAAGGGCCTTGAGTGGATTGGATATATTGATCCTTACTATGGTGATC
R Q A P G K G L E W I G Y I D P Y Y G D

                                     270                               300
CTGGCTACAGCCAGAAGTTCAAGGGCAAGGCCACATTGACTGTTGACAAGTCCACCAGCA
P G Y S Q K F K G K A T L T V D K S T S

                                     330                               360
CAGCCTACATGGAGCTCAGCAGCCTGAGGTCTGAGGACACTGCAGTCTATTACTGTGCAA
T A Y M E L S S L R S E D T A V Y Y C A

                                     390                               420
GACGTGGCAACTTCCCGTACTACTTTGACTACTGGGGCCAAGGCACCCTTGTCACAGTCT
R R G N F P Y Y F D Y W G Q G T L V T V

                                     448
CATCAGGTGAGTCCTCACAACCTCTAGA
S S
```

FIG. 12

Nucleotide sequence (SEQ ID NO:18) and deduced amino acid sequence (SEQ ID NO:19) of the light chain variable region (including the signal peptide sequence) of HuPAR34 in the mini exon.

```

                                     30                               60
ACGCGTCCACCATGAGGACCCCTGCTCAGTTTCTTGGTATCTTGTGCTCTGGTTTCCTG
      M R T P A Q F L G I L L L W F P

                                     90                               120
GTATCAAATGTGACATCCAGATGACCCAGTCTCCATCTTCCCTGTCTGCATCTGTTGGAG
G I K C D I Q M T Q S P S S L S A S V G

                                     150                               180
ACAGGGTCACTATCACTTGCAAAGCAAGTCAGGACATTAATAGCTATTTAAGCTGGTTCC
D R V T I T C K A S Q D I N S Y L S W F

                                     210                               240
AGCAGAAACCAGGGAAAGCTCCTAAGACCCTGATCTATCGTGCAAACAGATTGGTAGATG
Q Q K P G K A P K T L I Y R A N R L V D

                                     270                               300
GGGTCCCATCAAGATTCAGTGGCAGTGGATCTGGGCAAGATTATACTCTCACCATCAGTA
G V P S R F S G S G S G Q D Y T L T I S

                                     330                               360
GCCTGCAGCCTGAGGATTTGCAACTTATTATTGTCTACAGTATGATGAGTTTCCGTACA
S L Q P E D F A T Y Y C L Q Y D E F P Y

                                     390                               415
CGTTCGGAGGAGGGACCAAGGTGGAATAAAACGTAAGTGCACTTTCCTTCTAGA
T F G G G T K V E I K
```

FIG. 13

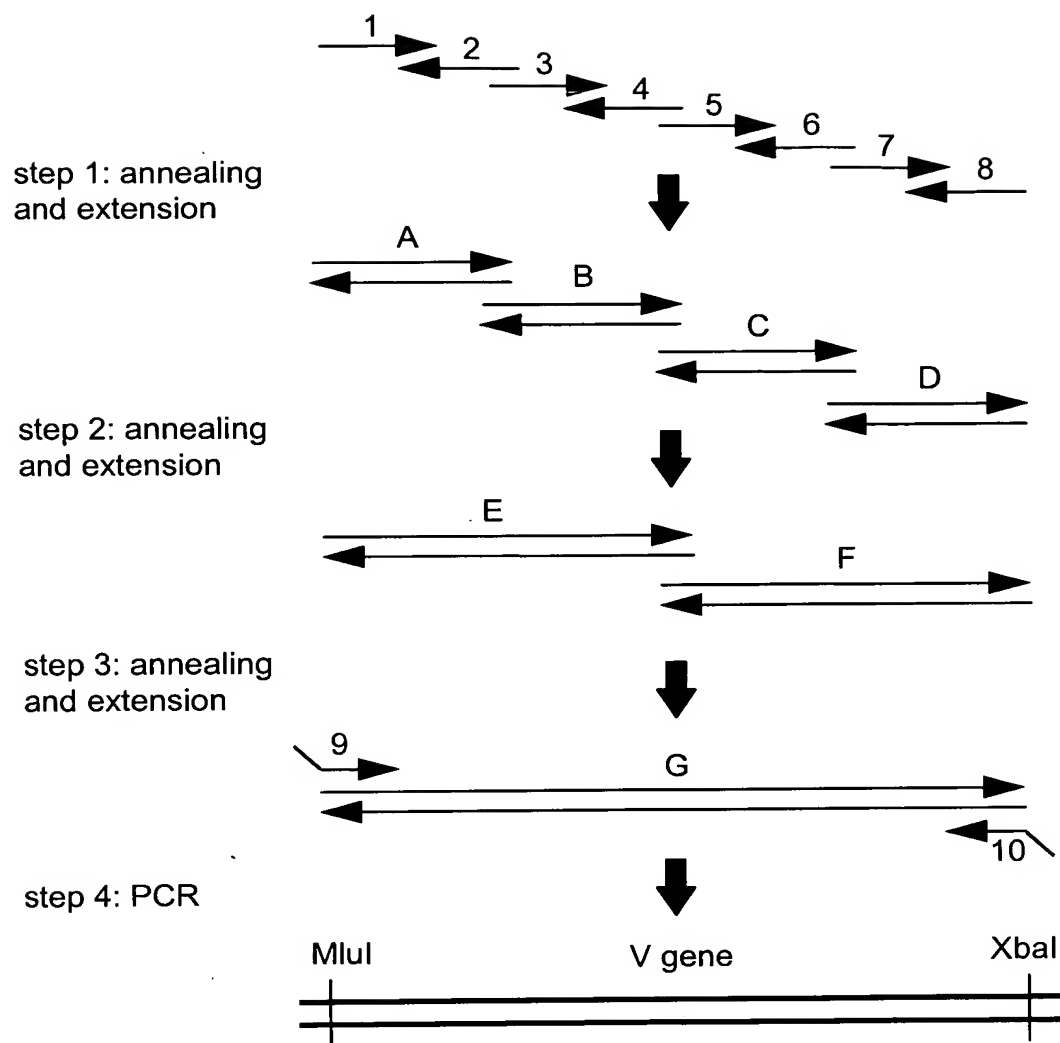


FIG. 14

Oligonucleotide primers used for the synthesis of the HuPAR34 VH gene.

Oligonucleotide 1 (SEQ ID NO:20)

5'-CTAGCCACGCGTCCACCATGGAATGGAGATGGATCTTTCTCTTCCTCCTGTCAGGAACTACAGGTGTCCACTCTG-3'

Oligonucleotide 2 (SEQ ID NO:21)

5'-TTCACAGAAGCCCCAGGCTTCTTCACCTCAGCTCCAGACTGCACCAGCTGGACCTCAGAGTGGACACCTGTAGTTCC-3'

Oligonucleotide 3 (SEQ ID NO:22)

5'-AAGCCTGGGGCTTCTGTGAAAATATCCTGCAAGGTTTCTGGTTATGCATTCACTAACTACAACATGTATTGGGTG-3'

Oligonucleotide 4 (SEQ ID NO:23)

5'-CCATAGTAAGGATCAATATATCCAATCCACTCAAGGCCCTTTCCAGGGGCTGCCTCACCCAATACATGTTGTAGTTAG-3'

Oligonucleotide 5 (SEQ ID NO:24)

5'-GGATATATTGATCCTTACTATGGTGATCCTGGCTACAGCCAGAAGTTCAAGGGCAAGGCCACATTGAC-3'

Oligonucleotide 6 (SEQ ID NO:25)

5'-TGTCTCAGACCTCAGGCTGCTGAGCTCCATGTAGGCTGTGCTGGTGGACTTGTCAACAGTCAATGTGGCCTTGCCCTTG-3'

Oligonucleotide 7 (SEQ ID NO:26)

5'-GCAGCCTGAGGTCTGAGGACACTGCAGTCTATTACTGTGCAAGACGTGGCAACTTCCCGTACTACTTTGACTACTGGGG-3'

Oligonucleotide 8 (SEQ ID NO:27)

5'-GACTCGTCTAGAGGTTGTGAGGACTCACCTGATGAGACTGTGACAAGGTGCCTTGGCCCCAGTAGTCAAAGTAGTACG-3'

Oligonucleotide 9 (SEQ ID NO:28)

5'-CTAGCCACGCGTCCACCATG-3'

Oligonucleotide 10 (SEQ ID NO:29)

5'-GACTCGTCTAGAGGTTGTGAG-3'

FIG. 15

Oligonucleotide primers used for the synthesis of the HuPAR34 VL gene.

Oligonucleotide 1 (SEQ ID NO:30)

5'-CTAGCCACGCGTCCACCATGAGGACCCCTGCTCAGTTTCTTGGTATCTTGTGCTCTGGTTTCCTGGTATC-3'

Oligonucleotide 2 (SEQ ID NO:31)

5'-CAACAGATGCAGACAGGGAAGATGGAGACTGGGTCATCTGGATGTCACATTGATACCAGGAAACCAGAGCAAC-3'

Oligonucleotide 3 (SEQ ID NO:32)

5'-CTTCCCTGTCTGCATCTGTTGGAGACAGGGTCACTATCACTTGCAAAGCAAGTCAGGACATTAATAGC-3'

Oligonucleotide 4 (SEQ ID NO:33)

5'-GATCAGGGTCTTAGGAGCTTCCCTGGTTTCTGCTGGAACCAGCTTAAATAGCTATTAATGTCCTGACTTGC-3'

Oligonucleotide 5 (SEQ ID NO:34)

5'-GAAAGCTCCTAAGACCCTGATCTATCGTGCAAACAGATTGGTAGATGGGGTCCCATCAAGATTCAGTGGCAGTGGATC-3'

Oligonucleotide 6 (SEQ ID NO:35)

5'-CCTCAGGCTGCAGGCTACTGATGGTGAGAGTATAATCTTGCCCAGATCCACTGCCACTGAATCTTG-3'

Oligonucleotide 7 (SEQ ID NO:36)

5'-CAGTAGCCTGCAGCCTGAGGATTCGCAACTTATTATTGTCTACAGTATGATGAGTTTCCGTACACGTTCGGAGG-3'

Oligonucleotide 8 (SEQ ID NO:37)

5'-GACTCGTCTAGAAGGAAAGTCACTTACGTTTTATTTCACCTTGGTCCCTCCTCCGAACGTGTACGGAAAC-3'

Oligonucleotide 9 (SEQ ID NO:38)

5'-CTAGCCACGCGTCCACCATG-3'

Oligonucleotide 10 (SEQ ID NO:39)

5'-GACTCGTCTAGAAGGAAAG-3'

FIG. 16

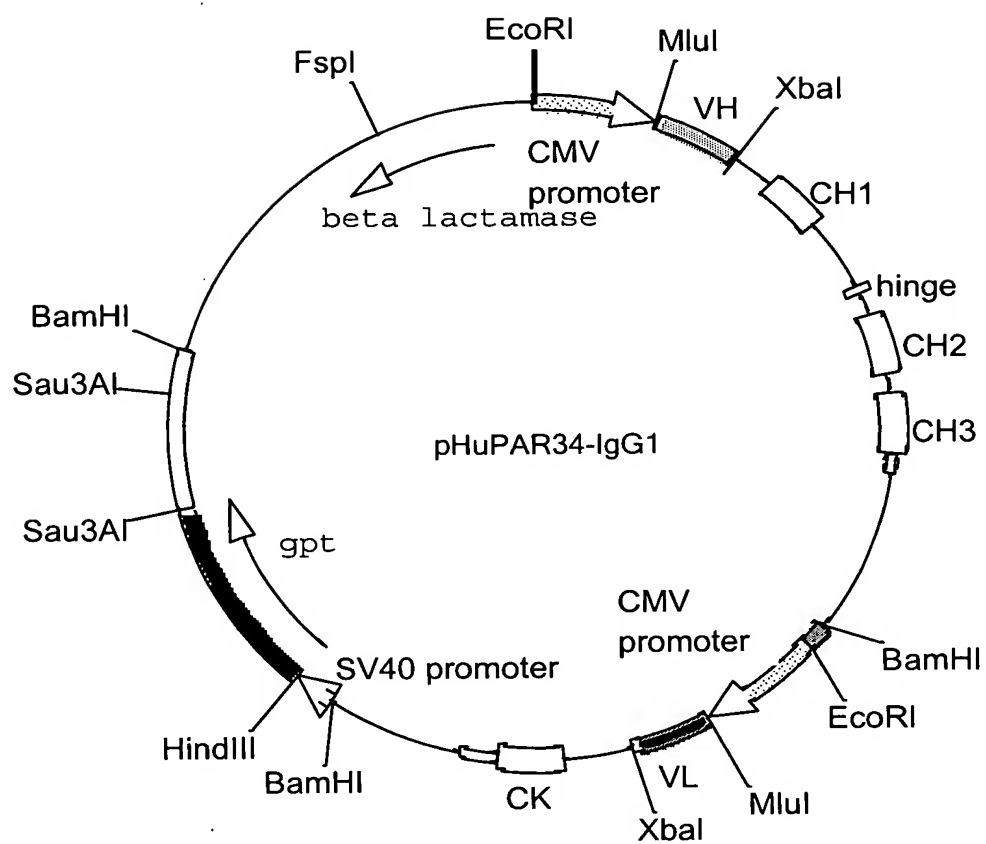


FIG. 17

Binding of Biotinylated MuPAR34 to Amphiregulin

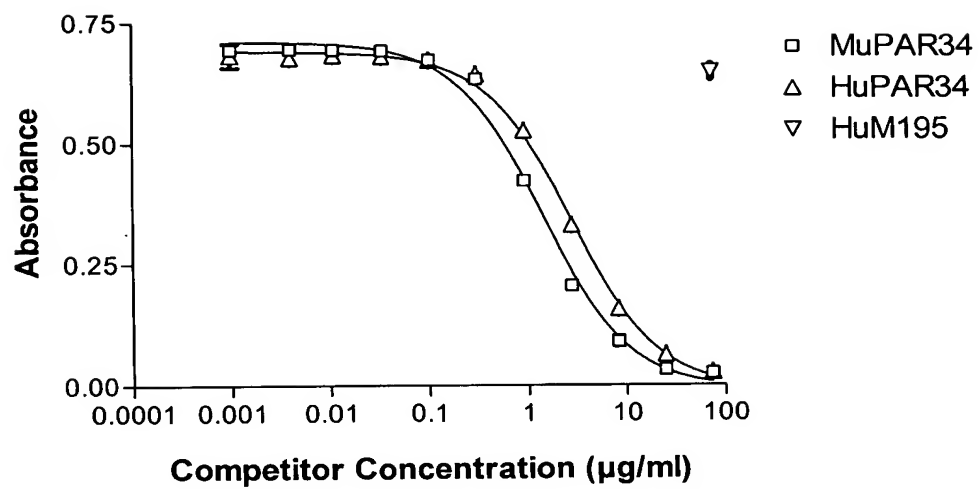
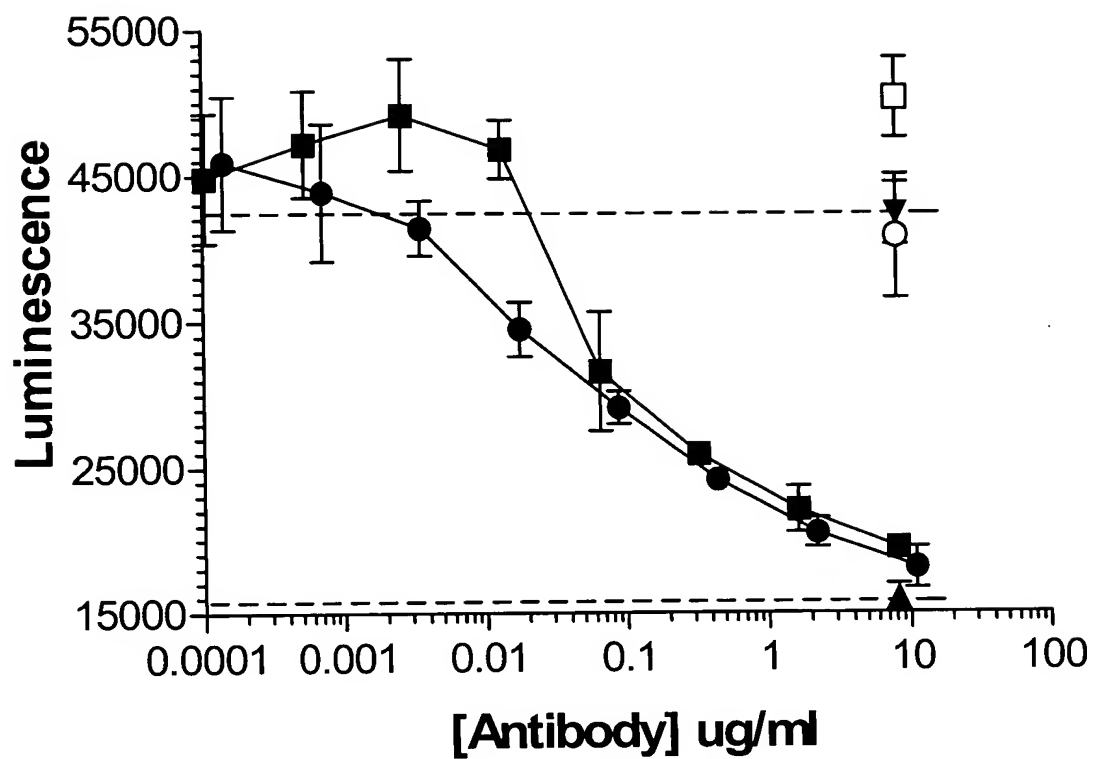


FIG. 18



$IC_{50}(\mu g/ml)^*$	
■ HuPAR34	0.055
● PAR34	0.025
□ Humanized IgG1 control	
○ Murine IgG2b control	
▼ Media Control	
▲ Mab225	

FIG. 19

HUMAN PSORIATIC SKIN/SCID MOUSE TRANSPLANT MODEL
EFFECT OF HuPAR34 ON NORMAL SKIN GRAFT

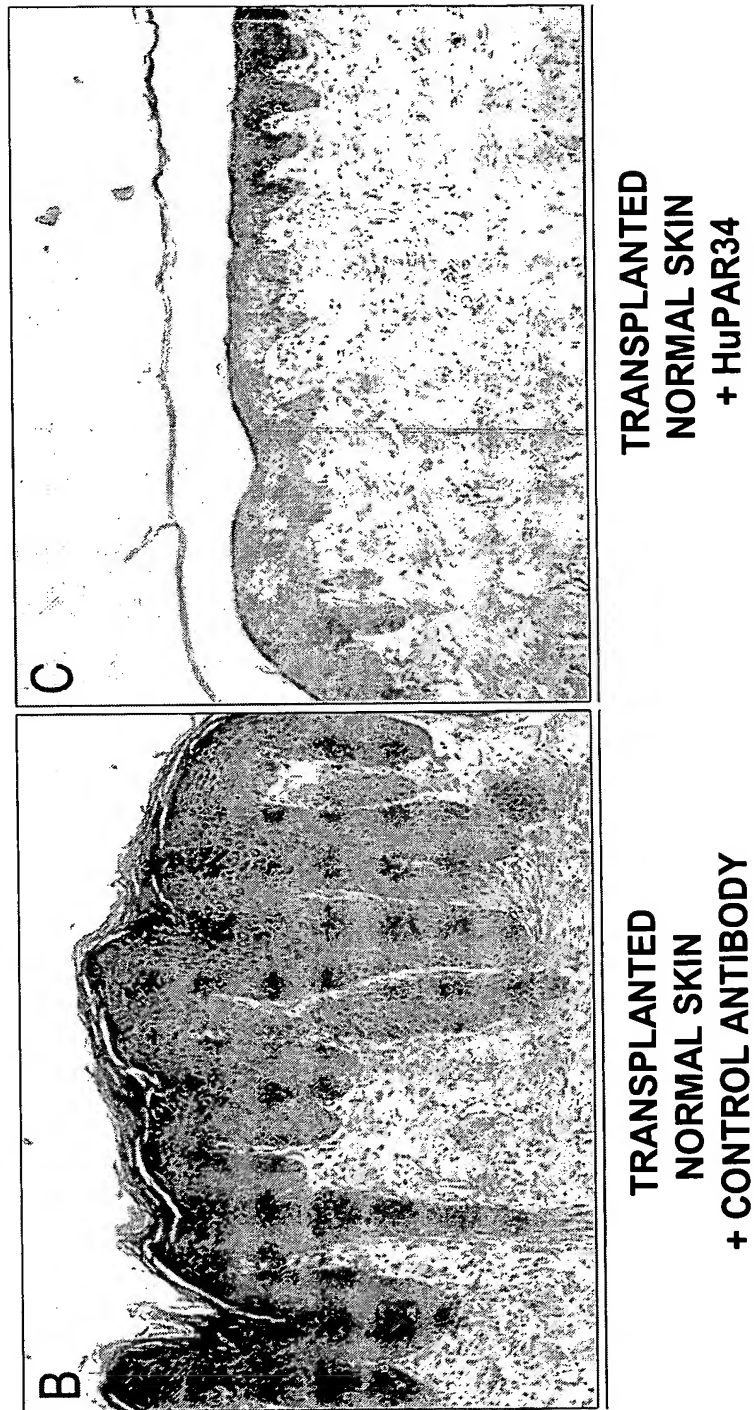


FIG. 20

**HUMAN PSORIATIC SKIN/SCID
MOUSE TRANSPLANT MODEL
EFFECT OF HuPAR34 ON PSORIATIC GRAFT**

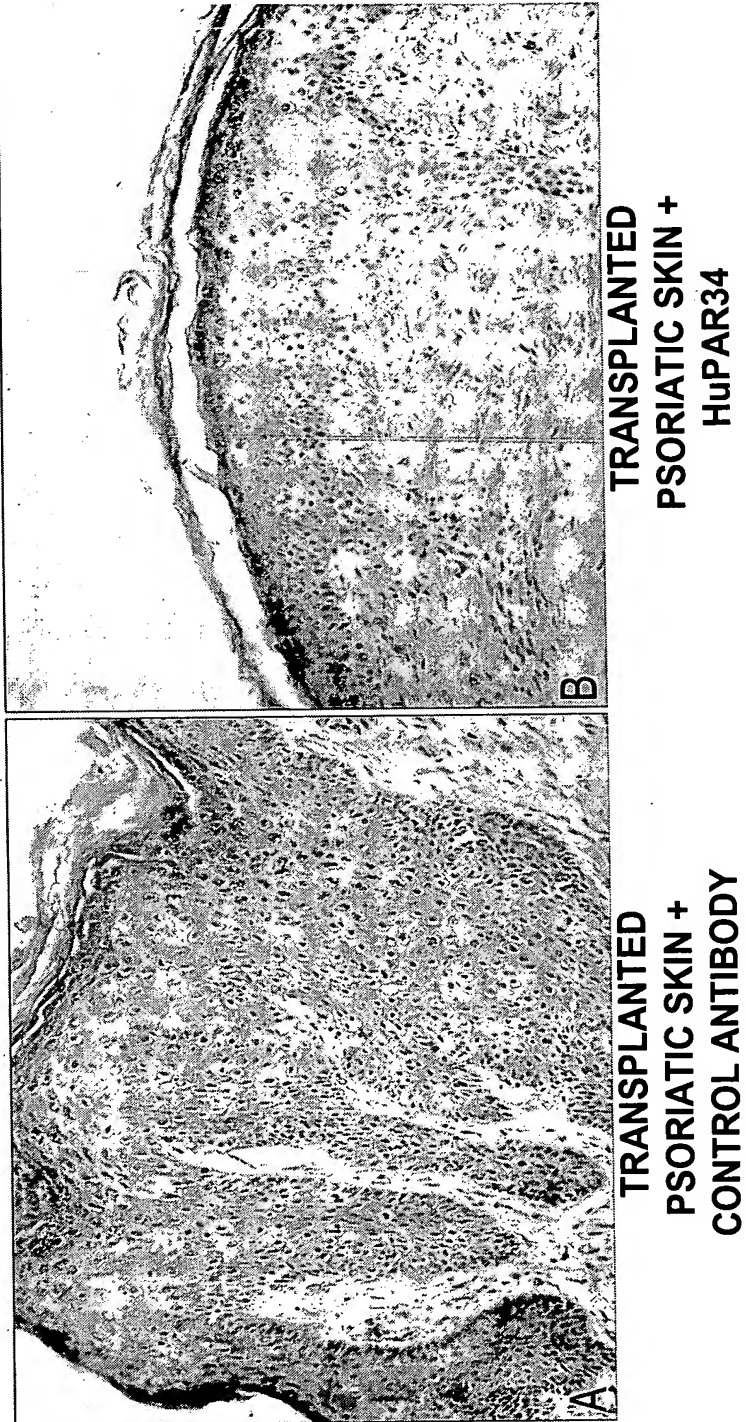
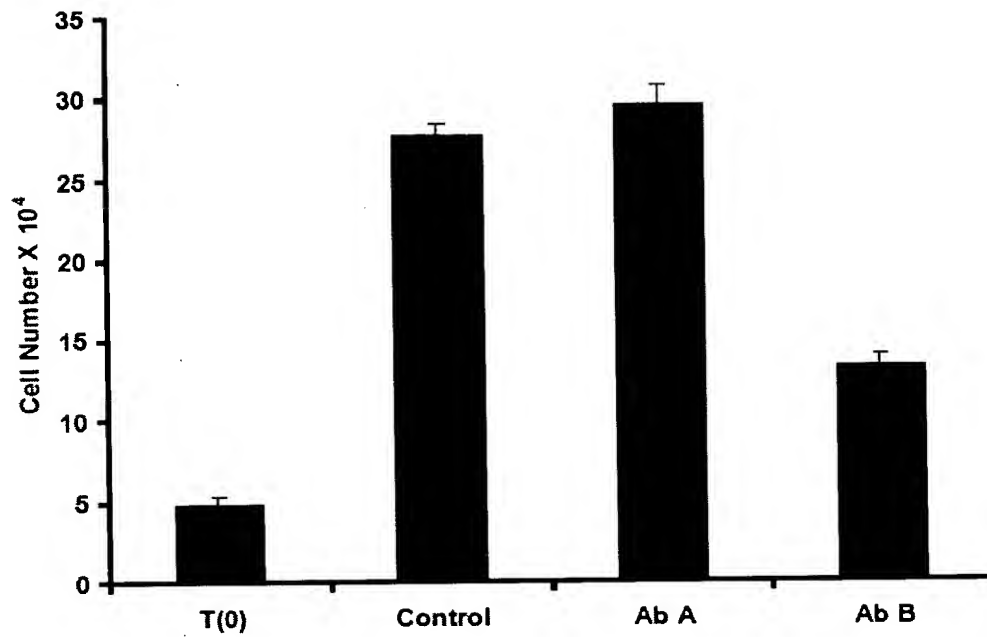


FIG. 21

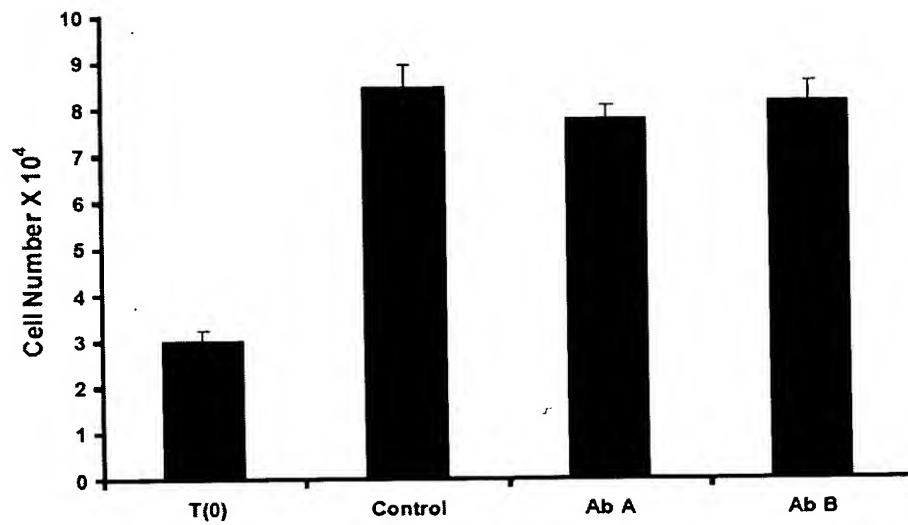
Cell Counts - Keratinocytes



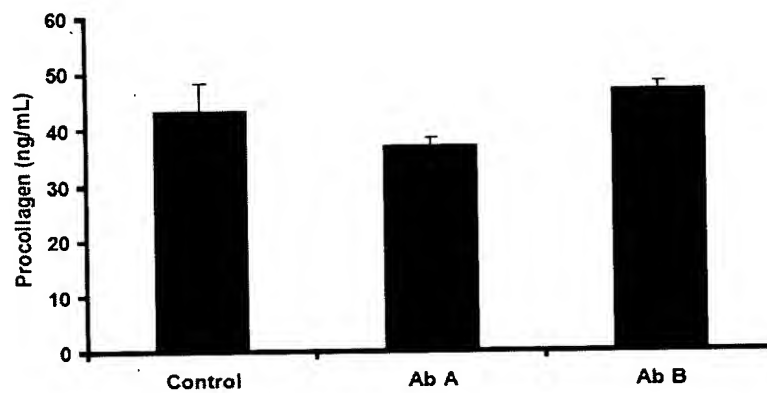
Control: KBM
Ab A: Control Antibody
Ab B: anti-amphiregulin antibody

FIG. 22

Cell Counts - Fibroblasts



Procollagen production - Fibroblasts



Control: KBM
Ab A: Control Antibody
Ab B: anti-amphiregulin antibody

FIG. 23